

Dear Editor

Evaluation of Latex Subclinical Sensitization by Way of the Basophil Activation Test and Specific IgE to Latex Recombinant Allergens

Latex allergy can cause severe adverse reactions. The diagnosis is difficult in many cases, because diagnostic tests are not always reliable.¹ Standardized extracts for prick tests can provide a sensitivity of 93%,² but some antigens are under-represented in these extracts,³ making specific IgE determination necessary in several cases. On the other hand, the specificity drastically decreases in patients allergic to pollen and mold owing to cross-reactivity between the latex profilin (rHev b 8) and enolase enzymes (rHev b 9), respectively.^{4,6} Patients allergic to latex can also have symptoms after ingestion of fruits with homologous proteins,⁷ and cross-reactivity carbohydrate determinants (CCDs) are also possible.⁸ With regard to provocation tests, the reproducibility of the latex glove-use test can be affected by the amount of allergenic latex protein present in the different gloves.¹ To solve cross-reactivity diagnostic questions, specific IgE to latex recombinant allergens can be determined, although its clinical relevance is not still clear. In this way, the Basophil Activation Test (BAT) was found to be more specific than specific IgE to latex in panallergen-sensitized patients.⁹

We studied ten patients with positive specific IgE

to latex who had a clinical history insufficiently indicative of allergy (Table 1), although latex allergy had been previously diagnosed at other medical centres. In cases 1, 2, 3, and 6, latex sensitization was found in studies of angioedema or urticaria episodes, which were finally attributed to food allergy. Cases 4, 8, and 10 experienced itching after using latex gloves. Case 5 had angioedema after surgical angioedema, which was finally attributed to drug allergy. Case 7 reported dyspnoea and eczema after using powdered latex gloves, but high sensitization to corn starch caused the symptoms. Case 9 was studied owing to family antecedents of latex allergy. The patients also had rhinoconjunctivitis and/or seasonal asthma owing to mold and pollen (Table 1).

As control groups, four latex-allergic patients, two of whom also had pollen-food-allergy-syndrome (PFAS), and two patients with PFAS only were studied.

The prick test with latex (Alk Laboratories, Madrid, Spain), and the prick-prick and latex glove use tests were performed in the series under re-study and in PFAS patients. The result was negative in all these cases. Specific IgE (Immuno-CAP, Thermo Scientific, MA, USA) for latex and its recombinant allergens were determined (rHev b 1, 3, 5, 6.01, 6.02, 8, 9, 11). In the group under re-study, ten patients had positive specific IgE to latex (Table 1), nine were positive for specific IgE to latex profilin (rHev b 8), and two were positive for specific IgE to rHev b 9. The result was negative for the remaining latex recombinant allergens. In the PFAS group, the specific IgE was posi-

Table 1 Clinical picture and specific IgE

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Clinical picture	U/Ae (food allergy) RNC/BA grass/ molds	U/Ae (food allergy) RNC/BA grass/ molds	U/Ae (food allergy) RNC/BA grass	Itching RNC/BA grass/ olea	Angioedema (drug allergy)	U/Ae (food allergy) RNC/BA grass	Corn allergy RNC/BA grass	Itching RNC/BA grass	Screening RNC/BA grass	Itching Erythema RNC/BA grass
Age (years)/gender	9/M	21/F	23/F	24/F	9/F	27/F	55/F	38/M	14/M	27/F
Total IgE (mU/ml)	1543	1361	39.1	170	232.1	102.9	75.2	296	801.7	342.2
Specific IgE										
slgE rPhl p 1 + 5 (kU/L)	>100	70.9	4.97	27.2	31.9	14.8	5.77	53.3	>100	25.2
slgE rPhl p 12 (kU/L)	10.6	10.1	1.05	1.41	8.51	Negative	Negative	2.25	6.53	4.32
slgE to ole 1 (kU/L)	75	1.64		1.55	4.78	Negative	0.78	3.9	5.21	Negative
slgE to alternaria (kU/L)	>100	18.3	NP	NP	NP	2.06	NP	NP	2.16	Negative
slgE latex (kU/L)	6.31	7.1	6.31	0.76	3.8	0.37	0.75	1.66	3.91	1.06
slgE rHev b 8 (kU/L)	12.1	Negative	1.62	2.59	15.5	1.13	0.48	3.28	18.9	3.78
slgE rHev b 9 (kU/L)	11.5	0.4	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
SlgE rHev b (1, 3, 5, 6.01, 6.02, 11)	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative

np, not performed; neg, negative. U/Ae, urticaria/angioedema; F, female, M, male; RNC, rhinoconjunctivitis, BA, bronchial asthma.

Table 2 Latex and pollen-food allergic patients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
	Allergic (Urtic/AE)	Allergic (Urtic/AE)	Allergic (AE) PFAS	Allergic (AE) PFAS	PFAS	PFAS
Age/gender	35/M	27/F	47/F	10/F	60/F	35/M
Comorbidity	RNC/BA (grass)	RNC/BA (dust)	Drug allergy	RNC/BA (grass)		RNC/BA (grass)
BAT						
Negative control	8.7%	7.0%	5.6%	13.3%	4.2%	6.7%
Positive control	63.1%	60.0%	65.5%	71.2%	68.8%	42.5%
Latex 2.5 ng/ml	18.0%	49.7%	60.5%	12.2%	2.3%	7.7%
Latex 5 ng/ml	25.0%	54.8%	66.2%	10.4%	4.2%	9.7%
Latex 10 ng/ml	32.0%	58.4%	74.4%	13.3%	3.6%	7.0%
Latex 25 ng/ml	51.5%	59.0%	77.5%	15.2%	3.8%	6.3%
Latex 50 ng/ml	62.2%	57.3%	81.0%	18.1%	9.4%	7.2%
Latex 100 ng/ml	73.0%	55.9%	69.5%	21.4%	3.8%	7.2%
Latex 500 ng/ml	84.6%	51.5%	67.7%	36.6%	3.6%	7.6%
Latex 1000 ng/ml	81.5%	47.4%	66.9%	43.6%	3.6%	8.5%
Latex 2000 ng/ml	84.2%	49.1%	65.4%	60.8%	3.6%	10.3%
Pirck test	Positive	Positive	Positive	Positive	Negative	Negative
Total IgE (UI/mL)	656.0	90.8	1021	467	550	120
Specific IgE						
Specific IgE latex (KU/L)	12.9	4.31	3.39	1.18	0.72	0.00
Specific IgE rHev b1 (KU/L)	0.02	0.62	0.03	0.00	0.00	0.00
Specific IgE rHev b3 (KU/L)	0.02	0.0	0.01	0.00	0.00	0.0
Specific IgE rHev b5 (KU/L)	11.1	1.27	0.01	0.00	0.00	0.1
Specific IgE rHev b6.01 (KU/L)	0.02	1.17	3.92	0.00	0.00	0.01
Specific IgE rHev b6.02 (KU/L)	0.00	6.0	3.94	0.00	0.00	0.00
Specific IgE rHev b8 (KU/L)	0.00	0.0	0.05	5.59	0.00	0.55
Specific IgE rHev b9 (KU/L)	0.00	0.0	0.04	0.00	0.00	0.01
Specific IgE rHev b11 (KU/L)	0.00	0.13	2.13	0.00	0.00	0.05

AE, angioedema; urtic, urticaria; BAT, basophil activation test; RNC, rhinoconjunctivitis; BA, bronchial asthma; M, male; F, female; PFAS, pollen-food-allergy-syndrome.

BAT results are given as the percentage of activated basophils after adding the stimulus. BAT results of the series of cases shown in Table 1 are negative, with activation values similar to those obtained in the PFAS group.

tive for latex in one case and for rHev b 8 in the other.

Prick tests and specific IgE were performed for fruits and vegetables involved in cross-reactivity syndromes with latex (banana, pineapple, avocado, kiwi, chestnuts, tomato, and potato), and other foods for which patients reported adverse reactions. Several cases had nut allergy (1, 2, 6, 7 and 8), fruit allergy (case 1, 3, 6, 7 and 8), tomato allergy (1 and 7), sea food allergy (Case 3), corn allergy (Case 7), and vegetable allergy (Case 8).

The BAT was performed in all cases in a dose-response curve with a latex-powdered, ammonium-free extract (Alk Laboratories). The assay was performed in accordance with the protocol previously described.¹⁰ The percentage of basophils expressing CD63 was the variable used to determine basophil ac-

tivation. A heparinised blood sample was drawn from the donors and aliquoted to test several stimuli. Each sample was tested with a negative control (serum saline), a positive control (the chemotactic peptide N-formylmethionyl-leucyl-phenylalanine), and the different latex concentrations (2.5, 5, 10, 25, 50, 100, 500, 1000 ng/ml).

For cell surface staining, monoclonal CD63-FITC and CD203c-PE were used (Beckman Coulter, CA, USA). After a lysing and washing process, samples were acquired by flow cytometer. The basophils were gated as CD203c-positive cells, as many as 800 events per sample. A test was considered positive if at least 17% of the basophils became activated after latex addition.⁹ It was previously assessed that the latex concentrations tested did not cause basophil activation in

five healthy controls. The BAT was negative for latex at all the concentrations tested in the ten cases of in vitro sensitized patients and in PFAS patients, and positive only for allergic patients (Table 2).

We decided to re-study this group of latex in vitro sensitized patients, previously diagnosed as allergic to latex, because the diagnosis was made using the method available years ago; skin prick test and specific IgE. However, none of these patients reported clear adverse reactions due to latex exposure, and experienced respiratory symptoms caused by grass or molds, both possibly involved in cross-reactivity phenomena with latex. Cross-reaction with fruits was also studied. Nevertheless, because latex allergy was finally rejected in the group, food allergy symptoms reported by the patients were attributed to a primary sensitization or cross-reactivity to grass pollens through rPhl p12 or other vegetable panallergens. Specific IgE to the bromelian-type carbohydrate was unavailable, but a higher sensitization rate was not expected in accordance with other studies.⁸

As had been suspected initially, the specific IgE to latex in this series could not be related to a positive *in vivo* provocation test, meaning a subclinical sensitization.

Consistent with these results, the specific IgE to latex determinants was only positive for those involved in cross-reactivity with grass pollens and molds, and the BAT was negative for all patients under re-study and those affected only by PFAS.

The possible clinical manifestations caused by latex sensitization must be carefully evaluated to establish clear indications with regard to latex contact avoidance, without causing unnecessary damage to the patient. The BAT can be of high utility in evaluating the risk of experiencing an adverse reaction in latex sensitized individuals, given its ability to detect a cellular response in real time, compared with sensitization with unknown clinical relevance shown by specific IgE.

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Ana Rodríguez Trabado¹,
Luis Miguel Fernández Pereira²,
Silvia Romero-Chala², José Antonio García-Trujillo²
and Carmen Cámara Hijón²

¹Allergy Department, Campo Arañuelo Hospital and
²Immunology Department, San Pedro de Alcántara
Hospital, Cáceres, Spain

Email: trabadoro@yahoo.es

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